**IN THE UNITED STATES DISTRICT COURT**
**FOR THE DISTRICT OF DELAWARE**

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| NIVAGEN PHARMACEUTICALS, INC.,<br><br>Plaintiff,<br><br>v.<br><br>AMNEAL PHARMACEUTICALS, INC., AMNEAL PHARMACEUTICALS of NEW YORK, LLC, AMNEAL PHARMACEUTICALS LLC, AMNEAL PHARMACEUTICALS PVT LTD., and AMNEAL EU, LTD.<br><br>Defendants. | ) | C.A. No. 24-846-GBW<br><br>**JURY TRIAL DEMANDED**<br><br>**PUBLIC VERSION** |

**NIVAGEN PHARMACEUTICALS, INC.'S REPLY BRIEF IN SUPPORT OF ITS MOTION FOR A TEMPORARY RESTRAINING ORDER AND FOR A PRELIMINARY INJUNCTION**

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## I. SUMMARY OF NIVAGEN'S ARGUMENTS IN REPLY

The Amneal Defendants should be enjoined from changing the status quo and launching their infringing potassium phosphate ready-to-use (RTU) product. First, Defendants present no non-infringement arguments concerning the '661 patent, and thus concede infringement. For the '291 patent, Defendants argue that the "nutrient/100 mL" limitations were not met under the doctrine of equivalents (DOE), but did not address Nivagen's actual point that the same amount of nutrients in an RTU product, delivered by either 100 mL or 250 mL of saline, would carry out the same function in the same way, achieving the same result.

Second, Defendants argue invalidity based on a 2019 FK package insert for a Fresenius concentrated product that requires dilution before administration. Defendants also argue that Nivagen had withheld this "highly material prior art" during patent prosecution. However, the patent examiner allowed both of the patents-in-suit over a prior art patent (Koneru) on low-aluminum, concentrated potassium phosphate solution. In essence, the examiner had already rejected Defendants' arguments, twice. Defendants' expert Dr. Amiji misconstrued what the Fresenius product was. In fact, as Dr. Jenke explains in reply, even after dilution, the Fresenius product would not be a sterile, RTU, or low aluminum product as the asserted claims require.

Third, Defendants argue that the '661 patent is not entitled to 2021 priority and is therefore anticipated by a 2022 "Pandya" publication. However, the 1.5-15 mmol range in the '661 patent claims are supported by the disclosures in the 2021 patent application that issued as the '291 patent. Defendants and Dr. Amiji focused only on the "1.5" number, but ignored disclosures such as "not more than 5.5 mmol/100 mL" and "not more than 2.7 mmol/100 mL" in the '291 patent. Defendants completely failed to address this 2021 written support for the claimed numeric *range*.

Fourth, Nivagen has established substantial, irreversible, immediate harm. The price erosion, loss of market share, and threat [redacted] are real and concrete harms that will occur without an injunction, and cannot be quantified.

## II. ARGUMENT

### A. Amneal's Product Will Infringe All Three Asserted Claims for This Motion

Defendants conceded their product would infringe claims 3 and 13 of the '661 patent. (D.I. 28 at 12). On the '291 patent, Defendants argue that, because the concentrations of nutrients in the asserted claim 11 are "2.5 times higher" than those in the accused product, there can be no infringement. (*Id.* at 7). However, Defendants never disputed Nivagen's point that, because the accused product contains 250 mL, which is 2.5 times the "100 mL" volume recited in the claim, the amount of nutrients in Defendants' product is identical to the claimed product. (D.I. 13 at 7). Both products deliver the same amount of nutrients but in different RTU volumes, and a POSA knows both volumes are in a range that is suitable for injection. (*Id.*). Neither Defendants nor Dr. Amiji disputed Dr. Rabinow's opinion that the additional volume of saline in Defendants' product "does not provide any additional and different meaningful change to the active ingredient … delivered to a patient." (D.I. 14 (Rabinow Decl.) at ¶ 60). Therefore, the same nutrients delivered in 250 mL volume are equivalent to those in the claimed 100 mL volume.

Defendants' argument that if a 100 mL product is diluted to 250 mL, the 100 mL product would not be "ready to use" misses the mark. (D.I. 28 at 8). Nivagen never argued for such a dilution of one RTU product to make another RTU product. What Dr. Rabinow actually pointed out is that the Fresenius concentrated product can be diluted into "100 to 250 mL of saline" before injection. (Rabinow Decl. at ¶ 57). This is evidence that the 100-250 mL range of volume is acceptable for injection, and saline in that volume range would carry out the same function of

carrying nutrients. (*Id.* at ¶¶ 59-60). Defendants and Dr. Amiji's argument is irrelevant to anything actually argued by Nivagen or Dr. Rabinow.

### B. Defendants Failed to Raise Any Question of Patent Invalidity

#### 1. The Fresenius Kabi Concentrated Product Is Very Different from the Claimed RTU Product, Before and After Dilution

Defendants argue that the Fresenius Kabi package insert (FK PI) is anticipatory. (D.I. 28 at 9 (middle para.), 10-12). Defendants argue that, once the FK product is diluted, it becomes "the ready-to-use forms" in the asserted claims. (*Id.* at 11). Not so. First, the "50 mcg/L aluminum" limitation in the claims cannot be met by diluting the FK concentrated product. According to Dr. Amiji, the FK concentrate would produce 45 mcg/L of aluminum in a 100 mL dilution. (D.I. 29 (Amiji Decl.) at ¶ 133). Yet, his calculation is based on a baseless assumption that the saline used in this dilution "contributes 0 or negligible amounts of aluminum." (*Id.*) As Dr. Jenke explains, with documented support, commercial salt products all contained aluminum, tens to more than 100 mcg/L. (Jenke Declaration filed herewith, ¶ 33). Furthermore, Dr. Amiji does not recognize that the new containers used for dilution and mixing would also contribute aluminum. (*Id.* at ¶¶ 35-36). If a glass container is used for the dilution process (e.g. a bottle), there could be 1000 mcg/L of aluminum in the solution, and the amount will increase over time. (*Id.*). Dr. Amiji's *ipse dixit* "reasonable assumption" of zero-aluminum dilution process is flatly wrong. (*Id.* at ¶ 34). In reality, "there is no basis for Dr. Amiji to conclude that a diluted … FK concentrate would contain less than 50 mcg/L of aluminum" at any point of time. (*Id.* at ¶ 37).

Second, beyond aluminum contents, a diluted preparation of the FK product is not sterile. One cannot reliably prevent contamination during the preparation. (Jenke Decl. at ¶ 27). The diluted preparation has a very short shelf life, and should be refrigerated due to its lack of sterility—and would not be considered by a POSA as "ready to use." (*Id.* at ¶¶ 27-28).

Defendants made only a cursory obviousness argument. (D.I. 28 at 11-12). This is not surprising because, as Dr. Amiji acknowledged, the patent examiner discussed a prior art patent ("Koneru") disclosing concentrated phosphate compositions with "low aluminum content" and about 1 mM/mL (i.e. 100 mmol/100 mL) of phosphorus, and issued the patents-in-suit over Koneru. (Amiji Decl. at ¶¶ 79, 88). The examiner concluded that "Koneru does not disclose or provide motivation to arrive at [the claimed subject matter in Nivagen's patents]." (*Id.*). In comparison, the FK product has a phosphorus concentration of 3 mmol/mL (*see* D.I. 29 Ex. K), which is ***three times*** that of Koneru and ***20 times*** that in the Nivagen patent claims.

As Dr. Jenke explains, a low-aluminum RTU product ensures sterility by eliminating a dilution process before injection, and minimizes aluminum content from additional saline or leaching from containers. (Jenke Decl. at ¶ 41). A diluted concentrate is "totally different" from a sterile, low-aluminum RTU product, and does not render the latter obvious. (*Id.* at ¶¶ 38-40).

**2. The Numeric Range in the '661 Patent Claims Has Adequate Written Support in the 2021 Patent Application**

The '661 patent is the second of two patents issued in the '291 patent family. (D.I. 28 at 5). Defendants argue that the "lower concentrations" within the '661 patent claims' 1.5 to 15 mmol/100 mL phosphorous concentrations range were first disclosed in 2023, but not in the 2021 application for the '291 patent. (*Id.* at 10). Defendants cite a single paragraph in the Amiji Declaration for support, which contains a conclusory statement that, "I reviewed a comparison of the [two patents], and the '291 patent does not include any written description that the phosphorous concentration can be as low as 1.5 mmol/100 mL." (Amiji Decl. at ¶ 112). But that is incorrect. The '291 patent discloses "more preferred embodiments" with phosphorus concentration at "not more than 2.7 mmol/100 ml" or "not more than 5.5 mmol/100 ml." (D.I. 1-1 (the '291 patent), col. 9, ll. 19-24, 28-33). Defendants and Dr. Amiji ignored these disclosures, which plainly refer to

"lower concentrations" in the claimed range, including the "as low as 1.5 mmol/100 mL" concentrations. If they meant that they could not find the number "1.5" in the '291 patent, they applied the wrong, "*in ipsis verbis*" legal standard, and their argument must fail. *See Rai Strategic Holdings, Inc. v. Philip Morris Products S.A.*, 92 F.4th 1085, 1090 (Fed. Cir. 2024) ("The specification need not expressly recite the claimed range to provide written description support.").

**3. Defendants' "Inequitable Conduct" Argument Is Baseless**

Defendants argue that the FK PI reference is "highly material," "anticipates and/or renders obvious" the asserted claims, but it was somehow withheld during prosecution. (D.I. 28 at 13). As discussed above in Part II.B.1, FK PI does not disclose aluminum content below 50 mcg/L *as diluted* because Defendants did not account for aluminum added from saline and containers. FK PI also does not disclose a sterile RTU product or solution, before or after the dilution process.

Fatal to Defendants' "highly material" characterization, the patent prosecution history clearly shows that FK PI would not have changed the examiner's mind. The examiner allowed both patents over Koneru. (*See* Amiji Decl. at ¶¶ 79, 88). Koneru disclosed a concentrated phosphate solution that requires dilution before use. (Batzer Decl. Ex. A, col. 20, ll. 2-8). Koneru disclosed aluminum at "even less than about 17 mcg/L" in the concentrate. (*Id.* at col. 4, lines 16-19). That is well below the 45 mcg/L amount *as diluted* for the FK product (which is still an underestimate, as discussed above). The FK concentrate contains up to 2000 mcg/L of aluminum. (Amiji Decl. at ¶ 133). Yet, after noting the "low aluminum" and "1 mM/mL phosphorous" disclosures from Koneru, the examiner allowed Nivagen's claims. (*Id.* at ¶¶ 79, 88). Defendants did not explain why disclosing the higher-aluminum FK product would have made any difference.

**C. Nivagen Will Suffer Irreparable Harm Without Injunctive Relief**

**1. Irreparable Harm Should Be Presumed**

Amneal relies heavily on a single statement in *Robert Bosch LLC v. Pylon Mfg. Corp*., 659 F.3d 1142, 1148-50 (Fed. Cir. 2011) for the proposition that *eBay Inc. v. MercExchange, L.L.C.*, 547 U.S. 388 (2006) "jettisoned the presumption of irreparable harm." However, *Bosch* also cautioned that *eBay* "did not expressly address the presumption of irreparable harm." *Bosch*, 659 F.3d at 1148. Furthermore, both *Bosch* and *eBay* dealt with a ***permanent*** injunction, issued at the conclusion of a case. In contrast, the present Motion seeks temporary, emergency relief, and is brought in the beginning of a lawsuit without the benefit of discovery. Under these circumstances, the presumption has not been jettisoned, and there is ample support that it should apply.

**2. Nivagen Will Suffer Irreparable Harm If Amneal Is Not Enjoined**

Notwithstanding any presumption, Nivagen has established substantial, irreversible, immediate harm. In response, Amneal advances two primary arguments: that Nivagen's harms are speculative and that damages can be quantified. (D.I. 28 at 16-19). These arguments lack merit.

**a. Nivagen's Harms are Concrete, Immediate and Real**

***First***, there is no legal support for Amneal's argument that any loss of market share, price erosion and other harms are speculative. The cases Amneal cited are inapposite. (D.I. 28 at 16). In *High Tech Med. Instrumentation, Inc. v. New Image Indus., Inc.*, 49 F.3d 1551, 1556 (Fed. Cir. 1995), the patentee relied entirely on the presumption of irreparable harm, but failed to show a likelihood of success on the merits. Furthermore, unlike here, there was no evidence whatsoever that the patentee sold or intended to sell a patented product. In *Gryphon Oilfield Sols, LLC v. Stage Completions (USA) Corp*, 2018 WL 447364, *4-5 (S.D. Tex. Jan. 17, 2018), the patentee had only conducted one failed field test on a prototype four years prior to moving for preliminary injunction. The court also noted that an injunction against the alleged infringer would likely destroy it as a viable company—a situation clearly not at issue here. *Id.* at *5.

***Second***, Amneal argues that Nivagen's loss of market share is "speculative" because it [redacted], but this argument also lacks merit. (D.I. 28 at 16-17). Nivagen has [redacted], obtained patents to protect its product, and [redacted] well before any trial on the merits through which Nivagen could be awarded damages. (Shukla Decl. at ¶¶ 3, 36; Malaspina Decl. ¶¶ 6, 12-14, 23-25). Here, there are several significant sources of harm that begin to accumulate immediately upon Amneal's entry, and that cannot be undone simply by withdrawing Amneal's product post-trial, [redacted] all of which threaten [redacted]. (Malaspina Decl. ¶¶ 4, 16-25).

In that regard, the cases cited by Amneal present very different facts than here. In *IGT v. Aristocrat Techs., Inc.*, 646 F. App'x 1015, 1018 (Fed. Cir. 2016), the irreparable harm was premised on the accused infringer filing an IPR petition and succeeding in cancelling the patentee's claims, but no petition had been filed much less instituted. The reputational harm in *Integra Lifesciences Corp. v. Hyperbranch Med. Tech., Inc.*, 2016 WL 4770244, at *18 (D. Del. Aug. 12, 2016) was based solely on the remote assumption that adverse events may occur in the unlikely event doctors were to use the accused product off-label. In *Sunoco Ptns. Mkt'g & Terminals L.P. v. Powder Springs Logistics, LLC*, 2018 WL 395750, at *6-7 (D. Del. Jan. 8, 2018), the harm was premised entirely on an assumption that defendants would blend butane to the "maximum" extent permitted by law—an assumption that, based on the evidence, was not borne out.

***Third***, Amneal attempts to downplay harm caused by price erosion, arguing that Nivagen's alleged price erosion is "speculative" because [redacted]. (D.I. 28 at 17-18). Amneal ignores Mr. Shukla's testimony—based on years of industry

experience in the relevant market—that lays out concrete, irreversible ways [redacted] in the event an injunction does not issue. (*See, e.g.*, Shukla Decl. ¶¶ 7-24). Additionally, Amneal's RTU Product [redacted] where customers are major purchasing consortiums who negotiate for long-term fixed price contracts, often with right of first refusal price-matching clauses. (Shukla Decl. at ¶¶ 10, 13-14, 18; Malaspina Decl. ¶¶ 11-13, 20-25). Basic economics [redacted] particularly where Amneal stands to lock up the market and make it impossible for price erosion to dissipate. (Malaspina Decl. ¶¶ 4, 20-31). Indeed, the Federal Circuit has held that [redacted].

Moreover, Amneal's citations for the proposition that price erosion is speculative because a price [redacted] has not yet been established have no merit. For example, in *SmartSky Networks, LLC v. Gogo Bus. Aviation, LLC*, 2024 WL 358136, at *5 (Fed. Cir. Jan. 31, 2024), the patentee's president conceded that he set reduced prices *before* the accused infringer announced the prices of its product. And, in *Nichia Corp. v. Everlight Americas, Inc.*, 855 F.3d 1328, 1342–43 (Fed. Cir. 2017), the court found that there were many competing players in the market and that several licensed competitors had offered products at lower prices, independent of the accused infringer, which drove market prices down. Here, [redacted]. (Malaspina Decl. ¶¶ 4, 20-25). Furthermore, [redacted] why the harms here will be particularly severe and difficult to quantify. (*Id.* ¶¶ 16-18, 27-31).

***Fourth***, Amneal entirely overlooks the harm regarding t [redacted] if an injunction does not issue. Instead, Amneal summarily dismisses this and other of Nivagen's allegations of harm, *e.g.*, loss of goodwill and reputation and the inability to recoup investment and advance R&D, on the basis that such harms are somehow inherently speculative. (D.I. 28 at 18). It is well-established that loss of goodwill, damage to reputation, and loss of business opportunities are all valid grounds for finding irreparable harm. *Aria Diagnostics, Inc. v. Sequenom, Inc.*, 726 F.3d 1296, 1304-1305 (Fed. Cir. 2013) (criticizing district court making no findings on harm that would accrue to patentee's R&D and investment in the technology, undermining work and money spent developing, validating, and commercializing any covered product, and remanding for further findings). Here, given [redacted] (Malaspina Decl. ¶¶ 23-25, 33-35).

In sum, Amneal's arguments and cited cases are readily dismissed. The harms alleged here—loss of market share, price erosion, and [redacted] are imminent and concrete, warranting at least a temporary injunction.

**b. Nivagen's Harms Are Unquantifiable**

Because Amneal dismisses the harms Nivagen stands to face, it asserts that Nivagen could adequately be compensated by money damages were it to prevail at trial. (D.I. 28 at 18-19). Not true. Certain of Nivagen's harms, [redacted] are unquantifiable. (Malaspina Decl. ¶¶ 4, 23-26). Other harms, such as loss of market share and price erosion, are also not quantifiable in view of t [redacted]

[redacted] following withdrawal by Amneal. (*Id.*, ¶¶ 27-31). Still other circumstances make the harm to Nivagen unquantifiable, including adverse impacts on [redacted] (*Id.*, ¶¶ 32-35).

**D. The Balance of Equities Favors Nivagen**

Amneal does not meaningfully address the balance of equities and instead asserts that Nivagen does not have a product on the market and if it did, "[i]t would be inequitable to hinder fair competition through invalid, not infringed, and unenforceable patents." (D.I. 28 at 19). But as already shown, Amneal will infringe Nivagen's valid and enforceable patents. [redacted] Amneal, on the other hand, is significantly larger than Nivagen, having a portfolio of more than 280 generic and specialty pharmaceuticals totaling in net sales of approximately $2.4 billion. (Malaspina Dec., ¶¶ 36-38). Further, Amneal could continue selling its vial formulation of potassium phosphate, so it would not entirely be out of the market. In view of these disparities, the equities favor Nivagen.

**E. The Public Interest Supports Injunctive Relief**

Amneal's primary argument concerning public interest is that the public would benefit from competition and lower prices. (D.I. 28 at 20). This argument lacks merit because, even with an injunction, [redacted]

## III. CONCLUSION

For the reasons stated herein and in Nivagen's opening brief, Nivagen respectfully requests that the Court grant its Motion.

Respectfully submitted,

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